WHAT IS CLAIMED IS:

1. An activatable imaging probe comprising a chromophore attachment moiety and one or more chromophores, wherein the chromophores are chemically linked to the chromophore attachment moiety so that upon activation of the imaging probe, the optical properties of the chromophores are altered, wherein the imaging probe is activated by phosphorylation, dephosphorylation, pH mediated cleavage, conformation change, enzyme-mediated splicing, enzyme-mediated transfer of the one or more chromophores, hybridization of a nucleic acid sequence to a complementary target nucleic acid, binding of the probe to an analyte, chemical modification of the chromophore, or binding of the probe to a receptor.

2. The probe of claim 1, wherein the optical properties of the chromophores are altered by dequenching, quenching, changes in wavelength, changes in fluorescence lifetime, changes in spectral properties, or changes in polarity or combinations thereof.

3. The probe of claim 1, wherein the chromophores are selected from the group consisting of fluorochromes, non-fluorescent chromophores, fluorescence quenchers, absorption chromophores, and combinations thereof.

4. An activatable imaging probe comprising a chromophore attachment moiety and one or more chromophores, wherein the chromophores are chemically linked to the chromophore attachment moiety so that upon activation of the imaging probe the optical properties of the chromophores are altered, wherein the probe is activated by phosphorylation or dephosphorylation of the probe.

5. The probe of claim 4, wherein the phosphorylation is mediated by a kinase.

6. The probe of claim 4, wherein the dephosphorylation is mediated by a phosphatase.

7. The probe of claim 4, wherein the probe comprises one or more phophorylation sites.

8. The probe of claim 7, wherein the chromophore attachment moiety comprises the one or more phosphorylation sites.

9. The probe of claim 7, wherein the one or more phosphorylation sites are within a spacer between the chromophore attachment moiety and the chromophores.

10. An activatable imaging probe comprising a chromophore attachment moiety and one or more chromophores, wherein the chromophores are chemically linked to the chromophore attachment moiety so that upon activation of the imaging probe the optical properties of chromophores are altered, wherein the probe is activated by receptor-mediated binding.

11. An imaging probe comprising a chromophore attachment moiety and one or more chromophores, wherein chromophores are chemically linked to the chromophore attachment moiety so that upon activation of the imaging probe the optical properties of the chromophores are altered, wherein the probe contains a receptor polypeptide specific for ligand binding.

12. The probe of claim 11, wherein the chromophore attachment moiety comprises the receptor polypeptide.

13. The probe of claim 11, wherein the receptor polypeptide is within a spacer between the chromophore attachment moiety and the chromophores.

14. An activatable imaging probe comprising a chromophore attachment moiety, a functional group, and one or more chromophores, wherein the chromophores are chemically linked to the chromophore attachment moiety so that upon activation of the probe the optical properties of the chromophores are altered, wherein the probe is activated by enzyme-mediated removal of the functional group from the probe.

15. The probe of claim 14, wherein the functional group is chemically linked to the chromophore attachment moiety.

16. The probe of claim 14, wherein the functional group is chemically linked to a spacer between the chromophore attachment moiety and the chromophores.

17. An activatable imaging probe comprising a chromophore attachment moiety and one or more chromophores, wherein chromophores are chemically linked to the chromophore attachment moiety so that upon activation of the imaging probe the optical properties of chromophores are altered, wherein the probe is activated by enzyme-mediated splicing.

18. The probe of claim 17, wherein the probe comprises a nucleic acid sequence specific for enzyme-mediated splicing.

19. The probe of claim 18, wherein the chromophore attachment moiety comprises the nucleic acid sequence specific for enzyme-mediated splicing.

20. The probe of claim 18, wherein the nucleic acid sequence specific for enzyme-mediated splicing is within a spacer between the chromophore attachment moiety and the chromophores.

21. The probe of claim 1, wherein the probe is activated by enzyme-mediated transfer of a chromophore.

22. An activatable imaging probe comprising a chromophore attachment moiety and one or more chromophores, wherein chromophores are chemically linked to the chromophore attachment moiety so that upon activation of the imaging probe the optical properties of chromophores are altered, wherein the probe contains a nucleic acid sequence specific for a recombinase.

23. The probe of claim 22, wherein the chromophore attachment moiety comprises the nucleic acid sequence specific for a recombinase.

24. The probe of claim 22, wherein the nucleic acid sequence specific for a recombinase is within a spacer between the chromophore attachment moiety and the chromophores.

25. An activatable imaging probe comprising a chromophore attachment moiety and one or more chromophores, wherein the chromophores are chemically linked to the chromophore attachment moiety so that upon activation of the imaging probe the optical properties of the plurality of chromophores are altered, wherein the probe contains a transmembrane signal sequence.

26. The probe of claim 25, wherein the chromophore attachment moiety comprises the transmembrane signal sequence.

27. The probe of claim 25, wherein the transmembrane signal sequence is derived from a TAT protein comprising a caspase-3 sensitive cleavage site.

28. The probe of claim 25, wherein the transmembrane signal sequence is Gly-Arg-Lys-Lys-Arg-Gln-Arg-Arg (SEQ ID NO:15) or Gly-Arg-Lys-Lys-Arg-Arg-Gln-Arg-Arg (SEQ ID NO:16).

29. The probe of claim 1, wherein the probe is activated by hybridization of a nucleic acid sequence to a complementary target nucleic acid.

30. The probe of claim 29, wherein the chromophore attachment moiety comprises the nucleic acid sequence.

31. The probe of claim 29, wherein the nucleic acid sequence is within a spacer between the chromophore attachment moiety and the chromophore.

32. The probe of claim 1, wherein activation occurs upon binding of the probe to an analyte.

33. The probe of claim 32, wherein the analyte is H^+, Ca^{2+}, Na^+, Mg^{2+}, Mn^{2+}, Cl^-, Zn^{2+}, O_2, NO, Fe^{2+}, K^+, or H_2O_2.

34. A method of *in vivo* optical imaging of a target in a subject, the method comprising:

(a) delivering to the subject an imaging probe of claim 1;

(b) allowing adequate time for the imaging probe to be activated within the target;

(c) illuminating the target with light of a wavelength absorbable by the chromophores;

(d) detecting a signal emitted by the chromophores; and

(e) forming an optical image from the emitted signal.

35. The method of claim 34, wherein steps (a) - (d) are repeated at predetermined intervals to enable evaluation of the emitted signal of the chromophores in the subject over time.

36. The method of claim 34, wherein the method is used to detect a disease in the subject.

37. The method of claim 34, wherein the method is used to characterize a phenotype or genotype of a disease in the subject.

38. The method of claim 34, wherein the method is used to characterize the severity of a disease.

39. The method of claim 36, wherein the disease is selected from the group consisting of cancer, cardiovascular diseases, neurodegenerative diseases, immunologic diseases, autoimmune diseases, inherited diseases, infectious diseases, bone diseases, and environmental diseases.

40. An *in vivo* optical imaging method for the simultaneous imaging of two or more different targets in a subject, the method comprising:

(a) delivering to a subject two or more different imaging probes of claim 1, each probe comprising a chromophore attachment moiety and one or more chromophores whose emitted signals are distinguishable from the one or more chromophores on each other probe;

(b) allowing adequate time for molecules in the two or more targets to activate the imaging probes;

(c) illuminating the target with light of one or more wavelengths absorbable by the chromophores;

(d) detecting signals emitted by the chromophores; and

(e) forming an optical image of the two or more different targets from the emitted signals.

41. The method of claim 40, wherein steps (a) - (d) are repeated at predetermined intervals to enable evaluation of the emitted signal of the chromophores from the two or more probes in the subject over time.

42. An optical imaging method for assessing activity of an agent in a subject, the method comprising:

(a) administering to the subject an imaging probe of claim 1;

(b) allowing time for a molecule in a target tissue to activate the probe, if the molecule is present;

(c) illuminating the target tissue with light of a wavelength absorbable by the chromophores;

(d) detecting a signal emitted by the chromophores;

(e) forming an optical image from the emitted signal;

(f) administering to the subject the agent and repeating steps (a)-(e); and

(g) comparing the emitted signals and images of steps (d) and (e) over time or at a different agent dose to assess activity of the agent.

43. A method for determining the presence of a composition in a subject, the method comprising:

(a) administering to a subject an imaging probe of claim 1, wherein activation occurs in the presence of the composition;

(b) allowing time for the composition in a target to activate the probe, if the composition is present;

(c) illuminating the target with light of a wavelength absorbable by the chromophores; and

(d) detecting a signal emitted by the chromophores, wherein a signal indicates the composition is present.

44. The method of claim 43, wherein the composition is a drug.

45. The method of claim 43, wherein the composition is a polypeptide expressed by a gene.

46. The method of claim 43, wherein steps (a) - (d) are repeated at predetermined intervals to enable the evaluation of the emitted signal of the chromophores in the subject over time.

47. A method for assessing the effective dosage of an agent in a subject, the method comprising:

(a) administering to the subject the agent at a specific dosage;

(b) administering to the subject an imaging probe of claim 1;

(c) allowing time for a molecule in a tissue of the subject to activate the probe, if the molecule is present;

(d) illuminating the tissue with light of a wavelength absorbable by the chromophores; and

(e) detecting the signal emitted from the chromophores to assess whether the specific dosage was effective. 48. The method of claim 47, wherein steps (a)-(e) are repeated at a different specific dosage and the detected signals from step (e) are compared to determine which dosage is most effective.

49. An optical imaging method for guiding therapeutic interventions in a subject, the method comprising:

(a) administering to the subject an imaging probe of claim 1;

(b) allowing time for a molecule in a tissue of the subject to activate the probe, if the molecule is present;

(c) illuminating the tissue with light of a wavelength absorbable by the chromophores; and

(d) detecting and using a signal emitted from the chromophores to guide a therapeutic intervention.

50. The method of claim 49, wherein the therapeutic intervention is surgical intervention.

51. The method of claim 34, wherein the subject is a mammal.

52. The method of claim 34, wherein the subject is a human.

53. The method of claim 34, wherein the subject is an animal model of disease.

54. The method of claim 34, wherein the illuminating and detecting steps are done using an endoscope, a catheter, a tomographic system, surgical goggles with attached bandpass filters, or an intraoperative microscope.

55. An *in vitro* optical imaging method for assessing activity of an agent in a sample, the method comprising:

(a) administering to the sample an imaging probe of claim 1;

(b) allowing time for a molecule in the sample to activate the probe, if the molecule is present;

(c) illuminating the sample with light of a wavelength absorbable by the chromophores;

(d) detecting a signal emitted from the chromophores;

(e) forming an optical image from the emitted signal;

(f) administering to the sample the agent and repeating steps (a)-(e); and

(g) comparing the emitted signals and images of steps (d) and (e) over time or at different agent doses to assess the activity of the agent.